RESTRICTION REQUIREMENT

The Examiner has required restriction under 35 U.S.C. 121 to one of the following:

I. Claims 1-6 and 9-12 drawn to a polynucleotide, a vector, a host cell, classified under class 536, subclass 23.4;

II Claims 7 and 8 drawn to TNFSF-SPD fusion protein classified in class 530, subclass 387.3; and

III Claims 13-15 drawn to a method for stimulating immune response, classified in class 424, subclass 143.1.

Applicant provisionally elects, with traverse, to prosecute Group II, Claims 7 & 8, as required by the Examiner pending reconsideration of the restriction requirement.

REMARKS

These remarks are in response to the Office Action mailed March 22, 2000. Applicant respectfully traverses the Examiner's restriction requirements, and provisionally elects to prosecute Group II, Claims 7 & 8. Claims in Group I and Group III are reserved for potential Divisional applications.

Applicant respectfully requests reconsideration of the restriction requirement involving Groups I and II. The modification that Applicant requests is that the Group I claims (concerning the nucleotide version of the invention) and the Group II claims (concerning the protein version of the invention) be kept together in a single invention. Applicant reasons as follows:

This invention concerns the production of multimeric forms of TNF superfamily ligand proteins (such as CD40L) produced as *fusion* proteins with members of the collectin family of molecules (such as surfactant protein D or SPD).

The Examiner makes the reasonable point that a protein can be produced independently of its nucleotide sequence through chemical synthesis methods. Indeed, some rather large molecules have been produced through chemical synthesis. However, this has not been done for molecules like CD40L or SPD for the following reasons:

(1) CD40L must be in a homotrimeric conformation in order to be active.

(2) In addition, it is glycosylated and this cannot be readily done by chemical synthesis.

(3) There is no efficient method known to the art for achieving the necessary homotrimeric formation by the usual refolding methods employed for chemically synthesized proteins.

The problem is even greater for SPD which has twelve chains held together at a "hub" by disulfide bonds. The twelve chains are organized into four "arms", each of which is a collagen-like trimer. Because the collagen-like trimer is formed from repeats of an amino acid subunit, the three chains must be aligned in parallel for the molecule to function. In living cells, this alignment is achieved by a "registration peptide" sequence at the N-terminus of each chain, which causes the winding of the triple helix to initiate near the N-terminus of each chain. This type of assembly has not been duplicated outside of living cells, and it is necessary for the activity of the final protein in the invention.

Only living cells can produce a protein this complex, given the current limits on chemical synthesis. Living cells, such as the CHO cells used in the reduction to practice, require a nucleotide template to synthesize a protein. Therefore, Applicant asks that the Examiner consider the nucleotide sequences used to produce the proteins as part of the same invention as the proteins themselves (i.e., leaving the claims in Group I and II as a single invention).

For examination purposes, Applicant elects to use human CD40L-SPD as the species prototype, which was submitted in the application as a nucleotide sequence in SEQ ID No. 1 and as a protein sequence in SEQ ID No. 2.

Applicant does not traverse the Examiner's division of the Group III claims, and will file a divisional application on these."

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' representative can be reached at (760) 788-7401.

Respectfully submitted,

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